

**Claims**

[1] A chimeric recombinant binding domain-heterogeneous functional group fusion wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion [B-Ext-F], which is characterized by

5        adding functional group(F) at the end of extension peptide chain(Ext) connected to binding domain(B) ;

             having uncoupled Cysteine on said extension peptide chain(extension chain) at any of position 1~45 for disulfide bonding between two monomers to produce dimer.

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[2] A chimeric recombinant binding domain-heterogeneous functional group fusion wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion [B-Ext(L)-F], which is characterized by

             adding functional group(F) at the end of extension peptide chain(Ext)  
15        connected to binding domain(B) ;

             having uncoupled Cysteine on said extension peptide chain(extension chain) at any of position 1~45 for disulfide bonding between two monomers to produce dimer ;

             having the peptide linker(L) that comprises the amino acid sequence  
20        between the last Cysteine of said uncoupled Cysteines on extension chain and functional group(F)(the end of extension chain(Ext)) ;

             having 1~50 amino acids between the last Cysteine of said uncoupled Cysteines on extension chain and functional group(F).

25        [3] A chimeric recombinant binding domain-heterogeneous functional group fusion wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion [B-Ext(LAD)-F], which is characterized by

adding functional group(F) at the end of extension peptide chain(Ext)  
connected to binding domain(B) ;

having uncoupled Cysteine on said extension peptide chain(extension  
chain) at any of position 1~45 for disulfide bonding between two monomers to  
5 produce dimer ;

having the peptide linker(L) that comprises the amino acid sequence  
between the last Cysteine of said uncoupled Cysteines on extension chain and  
functional group(F)(the end of extension chain(Ext)) ;

said peptide linker(L) is a peptide linker containing an affinity domain  
10 (LAD) which has homomeric self affinity or heteromeric affinity making the  
domain to assemble and leading to the formation of homomeric multimer or  
heteromeric multimer domain ;

having 1~50 amino acids between the affinity domain(AD) in peptide  
linker and functional group(F).

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[4] A chimeric recombinant binding domain-heterogeneous functional group  
fusion wherein the chimeric recombinant binding domain-extension peptide  
chain-functional group fusion [B-Ext(LFA)-F], which is characterized by

adding functional group(F) at the end of extension peptide chain(Ext)  
20 connected to binding domain(B) ;

having uncoupled Cysteine on said extension peptide chain(extension  
chain) at any of position 1~45 for disulfide bonding between two monomers to  
produce dimer ;

having the peptide linker(L) that comprises the amino acid sequence  
25 between the last Cysteine of said uncoupled Cysteines on extension chain and  
functional group(F)(the end of extension chain(Ext)) ;

said peptide linker(L) is a flexible amino acid sequence peptide

linker(LFA) which contains non-bulky amino acids like Glycine(G) or Alanine(A) or Serine(S) or Glutamine(Q) or Glutamic acid(E) or Asparagine(N), Aspartic acid(D) ;

having 1~50 amino acids between the last Cysteine of said uncoupled  
5 Cysteines on extension chain and functional group(F).

[5] A chimeric recombinant binding domain-heterogeneous functional group fusion wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion [B-Ext(LADFA)-F], which is characterized by

10 adding functional group(F) at the end of extension peptide chain(Ext) connected to binding domain(B) ;

having uncoupled Cysteine on said extension peptide chain(extension chain) at any of position 1~45 for disulfide bonding between two monomers to produce dimer ;

15 having the peptide linker(L) that comprises the amino acid sequence between the last Cysteine of said uncoupled Cysteines on extension chain and functional group(F)(the end of extension chain(Ext)) ;

said peptide linker(L) is a peptide linker containing an affinity domain (LAD) which has homomeric self affinity or heteromeric affinity making the  
20 domain to assemble and leading to the formation of homomeric multimer or heteromeric multimer domain ;

said peptide linker(L) is also a flexible amino acid sequence peptide linker(LFA) which contains non-bulky amino acids like Glycine(G) or Alanine(A) or Serine(S) or Glutamine(Q) or Glutamic acid(E) or Asparagine(N), Aspartic  
25 acid(D) ;

having 1~50 amino acids between the affinity domain(AD) in peptide linker and functional group(F).

[6] A chimeric recombinant binding domain-heterogeneous functional group fusion which has binding domain(B) composed of multiple chains(B1,B2,B3,,,Bn) wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion [B1-Ext or Ext(L) or Ext(LAD) or Ext(LADFA), B2-F, B3,,,Bn], which is characterized by

having one of the chain(B1) of binding domain connected to extension peptide chain(Ext) ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer{B1-Ext};

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain {B1-Ext(L)} ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain, and said peptide linker(L) has an affinity domain(AD) which has homomeric self affinity or heteromeric affinity leading to the formation of homomeric multimer or heteromeric multimer domain{B1-Ext(LAD)} ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain, and said peptide linker(L) has an affinity domain(AD) which has homomeric self

affinity or heteromeric affinity leading to the formation of homomeric multimer or heteromeric multimer domain and said peptide linker(L) also comprises flexible amino acid sequence with non-bulky amino acids like Glycine(G) or Alanine(A) or Serine(S) or Glutamine(Q) or Glutamic acid(E) or Asparagine(N), Aspartic acid(D){B1-Ext(LADFA)} ;

having functional group(F) added to another chain(B2) which composes the binding domain{B2-F}.

[7] A chimeric recombinant binding domain-heterogeneous functional group fusion which has binding domain(B) composed of multiple chains(B1,B2,B3,,,Bn) wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion [B1-Ext or Ext(L) or Ext(LAD) or Ext(LADFA), B2-L-F, B3,,,Bn], which is characterized by

having one of the chain(B1) of binding domain connected to extension peptide chain(Ext) ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer{B1-Ext};

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain{B1-Ext(L)} ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain, and

said peptide linker(L) has an affinity domain(AD) which has homomeric self affinity or heteromeric affinity leading to the formation of homomeric multimer or heteromeric multimer domain{B1-Ext(LAD)} ;

5       said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain, and said peptide linker(L) has an affinity domain(AD) which has homomeric self affinity or heteromeric affinity leading to the formation of homomeric multimer or  
10   heteromeric multimer domain and said peptide linker(L) also comprises flexible amino acid sequence with non-bulky amino acids like Glycine(G) or Alanine(A) or Serine(S) or Glutamine(Q) or Glutamic acid(E) or Asparagine(N), Aspartic acid(D){B1-Ext(LADFA)} ;

      having functional group(F) added to peptide linker(L) connected from the  
15   end of another chain(B2) which composes binding domain and said peptide linker(L) comprises 1~50 amino acids{B2-L-F}.

[8] A chimeric recombinant binding domain-heterogeneous functional group fusion which has binding domain(B) composed of multiple chains(B1,B2,B3,,,Bn)  
20   wherein the chimeric recombinant binding domain-extension peptide chain-functional group fusion[B1-Ext or Ext(L) or Ext(LAD) or Ext(LADFA), B2-LFA-F, B3,,,Bn], which is characterized by

      having one of the chain(B1) of binding domain connected to extension peptide chain(Ext) ;

25       said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer{B1-Ext};

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain{B1-Ext(L)} ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain, and said peptide linker(L) has an affinity domain(AD) which has homomeric self affinity or heteromeric affinity leading to the formation of homomeric multimer or heteromeric multimer domain{B1-Ext(LAD)} ;

said extension peptide chain(extension chain) has uncoupled Cysteine at any of position 1~45 for disulfide bonding between two monomers to produce dimer and contains peptide linker(L) that comprises the amino acid sequence from the last Cysteine of said uncoupled Cysteines to the end of extension chain, and said peptide linker(L) has an affinity domain(AD) which has homomeric self affinity or heteromeric affinity leading to the formation of homomeric multimer or heteromeric multimer domain and said peptide linker(L) also comprises flexible amino acid sequence with non-bulky amino acids like Glycine(G) or Alanine(A) or Serine(S) or Glutamine(Q) or Glutamic acid(E) or Asparagine(N), Aspartic acid(D){ B1-Ext(LADFA)} ;

having functional group(F) added to peptide linker(L) connected from the end of another chain(B2) which composes binding domain and said peptide linker(L) is LFA comprising flexible amino acid sequence with non-bulky amino acids like Glycine(G) or Alanine(A) or Serine(S) or Glutamine(Q) or Glutamic acid(E) or Asparagine(N), Aspartic acid(D) and said peptide linker(L) comprises

1~50 amino acids {B2-LFA-F}.

[9] A dimer of chimeric recombinant binding domain-heterogeneous functional group fusion characterized in that the uncoupled Cysteine on the extension chain  
5 (Ext) of chimeric recombinant binding domain-extension chain-functional group fusion (B-Ext-F) as defined in any one of claims 1 to 8 forms disulfide-bond-bridge to make dimers by oxidation with the uncoupled Cysteine on extension chain of binding domain-extension chain fusion (B-Ext) as defined in any one of claims 1 to 8 or with uncoupled Cysteine on the extension chain of chimeric  
10 recombinant binding domain- extension chain-functional group fusion(B-Ext-F) as defined in any one of claims 1 to 8.

[10] The chimeric recombinant binding domain-heterogeneous functional group fusion according to any one of claims 1 to 8, characterized in that the order of  
15 protein domain from amino terminal to carboxyl terminal is binding domain-extension chain-functional group(B-Ext-F).

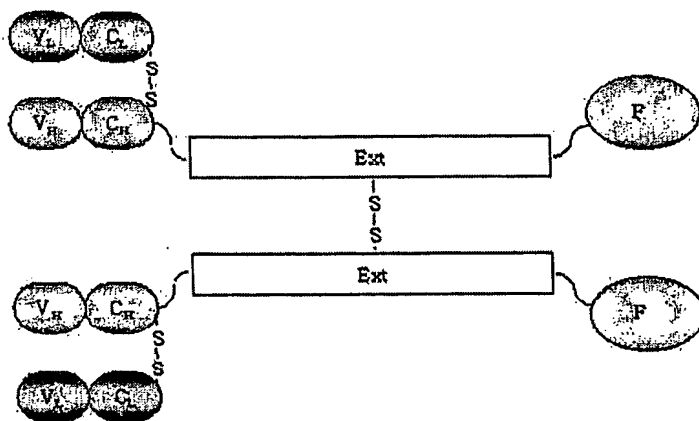
[11] The chimeric recombinant binding domain-heterogeneous functional group fusion according to any one of claims 1 to 8, characterized in that the order of  
20 protein domain from amino terminal to carboxyl terminal is functional group-extension chain-binding domain (F-Ext-B).

[12] The chimeric recombinant binding domain-heterogeneous functional group fusion according to any one of claims 1 to 8, characterized in that the binding  
25 domain is amino acid sequence which compose antibody or fragments of antibody or fragments of antibody affinity.



[13] The chimeric recombinant binding domain-heterogeneous functional group fusion according to any one of claims 1 to 8, characterized in that binding domain is Fab fragment of antibody.

- 5 [14] The chimeric recombinant binding domain-heterogeneous functional group fusion according to any one of claims 1 to 8, characterized in that binding domain has structure as below,

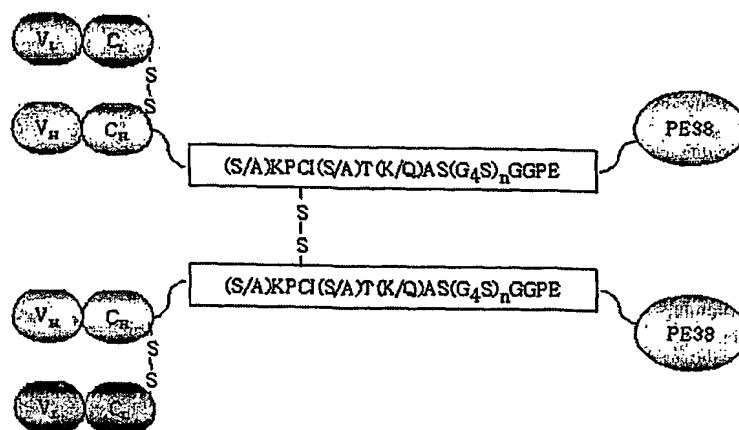


According to the structural formula of protein above,

- 10 V<sub>L</sub> is variable region on light chain of monoclonal antibody;  
 C<sub>L</sub> is constant region on light chain of monoclonal antibody;  
 V<sub>H</sub> is variable region on heavy chain of monoclonal antibody;  
 C<sub>H</sub> is constant region 1 on heavy chain of monoclonal antibody.

- 15 [15] The chimeric recombinant binding domain-heterogeneous functional group fusion according to any one of claims 1 to 8, characterized in that binding domain has structure as below,

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According to the structural formula of protein above,

$V_L$  is variable region on light chain of monoclonal antibody;

$C_L$  is constant region on light chain of monoclonal antibody;

5  $V_H$  is variable region on heavy chain of monoclonal antibody;

$C_H$  is constant region 1 on heavy chain of monoclonal antibody;

A is Alanine;

C is Cysteine;

E is Glutamic acid;

10 G is Glycine;

I is Isoleucine;

K is Lysine;

P is Proline;

Q is Glutamine;

15 S is Serine;

T is Threonine;

n is 1 or 2 or 3;

PE38 is 38kDa exotoxin derivative of *Pseudomonas aeruginosa* which

has been truncated of amino acid sequences of domain I and II that

20 are not required for cytotoxicity

[16] A polypeptide used in production of chimeric recombinant binding domain-heterogeneous functional group fusion as defined in any one of claims 1 to 8.

- 5 [17] A recombinant plasmid which codes polypeptide used in production of chimeric recombinant binding domain-heterogeneous functional group fusion as defined in any one of claims 1 to 8.

- 10 [18] A host cell having recombinant plasmid which codes polypeptide used in production of chimeric recombinant binding domain-heterogeneous functional group fusion as defined in any one of claims 1 to 8.

- 15 [19] A pharmaceutical composition which contains chimeric recombinant binding domain-heterogeneous functional group fusion as defined in any one of claims 1 to 8.

[20] A method for producing chimeric recombinant binding domain-heterogeneous functional group fusion as defined in any one of claims 1 to 8.